

U.S. DEPARTMENT OF COMMERCE PATENT & TRADEMARK OFFICE

95 Rec'd PCT/PTO 10 FEB 2000

B/O Form PTO-1390		Transmittal Letter to the United States Designated/Elected Office (DO/EO/US) Concerning a Filing Under 35 USC 371		Attorney's Docket Number REF/LIGNELL/551	
International Application Number PCT/EP99/07551		International Filing Date October 8, 1999		U.S. Application Number (if known) 09/463958	
Title of Invention TREATMENT OF DYSPEPSIA					
Applicant(s) for DO/EO/US Ake LIGNELL					

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items under 35 USC 371:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 USC 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 USC 371.
3. ☒ This express request to begin national examination procedures (35 USC 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 USC 371(b) and PCT Articles 22 and 39(1).
4. ☐ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ☐ A copy of the International Application as filed 35 USC 371(c)(2).
 - a. ☒ is transmitted herewith (required only if not transmitted by the International Bureau).
 - b. ☐ has been transmitted by the International Bureau.
 - c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☐ A translation of the International Application into English (35 USC 371(c)(2)).
7. ☐ Amendments to the claims of the International Application under PCT Article 19 (35 USC 371(c)(3))
 - a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
 - b. ☐ have been transmitted by the International Bureau.
 - c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
 - d. ☒ have not been made and will not be made.
8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 USC 371(c)(3)).
9. ☒ An oath or declaration of the inventor(s) (35 USC 371(c)(4)). (☐ Executed ☒ Unexecuted)
10. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 USC 371(c)(5)).

Items 11 to 16 below concern other document(s) or information included:

11. ☒ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☒ A **FIRST** preliminary amendment.
 - ☐ A **SECOND** or **SUBSEQUENT** preliminary amendment.
14. ☐ A substitute specification.
15. ☐ A change of power of attorney and/or address letter.
16. ☐ Other items or information:

Application Number (if Known) 09/463958		International Application Number PCT/EP99/07551		Attorney's Docket Number REF/LIGNELL/551	
				Calculations	PTO USE ONLY
17. The following fees are submitted: Basic National Fee (37 CFR 1.492(a)(1)-(5)): <input type="checkbox"/> Search report has been prepared by the EPO or JPO \$840.00 <input type="checkbox"/> International Preliminary Examination Fee paid to USPTO (37 CFR 1.482) \$670.00 <input type="checkbox"/> No International Preliminary Examination Fee paid to USPTO (37 CFR 1.482) but International Search Fee paid to USPTO (37 CFR 1.445(a)(2)) \$760.00 <input checked="" type="checkbox"/> Neither International Preliminary Examination Fee (37 CFR 1.482) nor International Search Fee (37 CFR 1.445(a)(2)) paid to USPTO \$970.00 <input type="checkbox"/> International Preliminary Examination Fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4) \$96.00				\$970.00	
ENTER APPROPRIATE BASIC FEE AMOUNT				\$ 970.00	
Surcharge of \$130.00 for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(e)).					
CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total Claims	7 -20 =	0	× \$18.00	\$ 0.00	
Independent Claims	1 -3 =	0	× \$78.00	\$ 0.00	
Multiple Dependent Claims (if applicable)			+ \$260.00		
TOTAL OF ABOVE CALCULATIONS				\$ 0.00	
Reduction by ½ for filing by small entity, if applicable. Verified Small Entity Statements must also be filed (Note 37 CFR 1.9, 1.27, 1.28)					
SUBTOTAL					
Processing fee of \$130.00 for furnishing the English translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(f)).					
TOTAL NATIONAL FEE					
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property.					
TOTAL FEES ENCLOSED				\$ 970.00	
				Refunded:	
				Charged:	

- a. ☒ A check in the amount of \$970.00 to cover the fees is enclosed.
- b. ☐ Please charge my Deposit Account Number 02-0200 in the amount of \$_____ to cover the above fees.
A duplicate copy of this sheet is enclosed.
- c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account Number 02-0200. A duplicate copy of this sheet is enclosed.

Note: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

BACON & THOMAS, PLLC
 625 SLATERS LANE - FOURTH FLOOR
 ALEXANDRIA, VIRGINIA 223124-1176
 (703) 683-0500

DATE: February 10, 2000

Respectfully submitted,

Richard E. Fichter

Richard E. Fichter
 Attorney for Applicant
 Registration Number: 26,382

09 / 4 6 3 9 5 8

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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Ake LIGNELL

U.S. National Phase of PCT/EP99/07551

Entry papers filed herewith February 10, 2000

For: TREATMENT OF DYSPEPSIA

Attention: PCT OFFICE

**PRELIMINARY AMENDMENT
AND INFORMATION DISCLOSURE STATEMENT**

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

The present application is the U.S. national phase of international application number PCT/EP99/07551. The following amendments pertain to the claims as amended.

Please amend the above-identified application as follows:

IN THE CLAIMS:

Please cancel claims 1-7 without prejudice or disclaimer.

REMARKS

Applicants have amended the claims in order to cancel the improper use claims. Applicants retain the right to reintroduce any subject matter canceled by the present Amendment at any time during the prosecution of this application or any further application claiming benefit of this application.

Applicants are submitting herewith a copy of the Swedish Patent Search Report which issued on International Application No. PCT/EP99/07551, of which the present application is the U.S. national phase. All of the publications cited in the Swedish

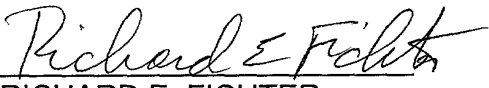
Patent Search Report are listed on the attached Form PTO-1449. There has not yet been any search performed by EPO with regard to this application.

The Examiner is respectfully requested to return an initialed and dated copy of the attached Form PTO-1449 to confirm that all publications listed thereon have been considered and made officially of record in the file of this application.

Applicants understand that, under the procedures of the PCT, a copy of the priority document (9803541-3, filed October 16, 1998) will have been supplied to the U.S. Patent Office pursuant to Rule 17 of the PCT Regulations. It is therefore respectfully requested that the first Official Action in the present application contain an indication that the appropriate priority document is in the file of this application.

In view of the above amendments, an early action on the application is now in order and is most respectfully requested.

Respectfully submitted,
BACON & THOMAS, PLLC

By: 
RICHARD E. FICHTER
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REF:kdd
PCTPRELI.AMD.wpd

DATE: February 9, 2000

29805/BN

TREATMENT OF DYSPEPSIA

5 The present invention relates to treatment of dyspepsia. The invention is particularly concerned with the use of at least one type of xanthophylls for the preparation of a medicament for prophylactic and/or therapeutic treatment of dyspepsia, and a method of treating dyspepsia. A preferred xanthophyll is astaxanthin.

10 Background of the invention

Dyspepsia, or indigestion, is one of the most common gastrointestinal disorders or diseases in both animals and humans. Dyspepsia is persistent or recurrent abdominal pain or abdominal discomfort centered in the upper abdomen. Dyspepsia refers to symptoms in the upper abdomen that are considered to be related to the upper alimentary tract. Often dyspepsia
15 is temporary and disappears spontaneously. In case alleviation of the symptoms is desired, ingestion of antacids is often the first choice of treatment. Antacids are normally not taken prophylactically.

However, there are several alternative therapeutic treatments of dyspepsia, and the present invention provides a new alternative, which may also be used for prophylactic
20 treatment.

Description of the invention

The present invention is directed to the use of at least one type of xanthophylls for the preparation of a medicament for prophylactic and/or therapeutic treatment of
25 dyspepsia.

In a preferred embodiment the xanthophyll is astaxanthin, especially astaxanthin in a form esterified with fatty acids. The astaxanthin in esterified form is suitably provided in the form of algal meal prepared from a culture of the alga *Haematococcus sp.*

The medicament may further comprise carbohydrate structures, such as
30 lipopolysaccharides, polysaccharides and glycoproteins, and/ or one or several different antioxidant(s), such as ascorbic acid (vitamin C) and tocopherol (vitamin E).

The medicament is preferably in the form of unit doses adapted for a daily dosage of xanthophyll(s) in the range of 0.05 to 1 mg per kg body weight of an individual, which is an animal or a human.

The invention is also directed to a method of prophylactic and/or therapeutic treatment of dyspepsia in an individual, which comprises administration to said individual of an dyspepsia-alleviating amount of a medicament comprising at least one type of xanthophylls.

5 In a preferred embodiment the xanthophyll is astaxanthin, especially astaxanthin in a form esterified with fatty acids. The astaxanthin in esterified form is suitably provided in the form of algal meal prepared from a culture of the alga *Haematococcus* sp.

The medicament may further comprise carbohydrate structures, such as lipopolysaccharides, polysaccharides and glycoproteins, and/ or one or several different
10 antioxidant(s), such as ascorbic acid (vitamin C) and tocopherol (vitamin E).

Preferably, the dyspepsia-alleviating amount of the medicament comprises xanthophyll(s) in the range of 0.05 to 1 mg per kg body weight of the individual, which is an animal or a human.

The at least one type of xanthophylls that are used in the present invention may
15 comprise a mixture of different types of xanthophylls or different forms of the same xanthophyll, such as a mixture of synthetic astaxanthin and naturally produced astaxanthin.

The mechanism of the prophylactic and therapeutic effect of the xanthophylls in the treatment of dyspepsia is not known, but it should be noted that they possess strong antioxidative properties and that they are soluble in fats and oils.

20 At present, the most preferred embodiment of the invention comprises algal meal having astaxanthin in esterified form with fatty acids dissolved in small droplets of naturally occurring oil and naturally occurring carbohydrate structures in the partially disrupted cell walls.

The medicament used in the invention may comprise additional ingredients
25 which are pharmacologically acceptable inactive or active in prophylactic and/or therapeutic use, such as flavoring agents.

The medicament may be presented in a separate unit dose or in mixture with food. Examples of separate unit doses are tablets, gelatin capsules and predetermined amounts of solutions, e. g. oil solutions, or emulsions, e.g. water-in- oil or oil-in-water emulsions.

30 Examples of foods in which the preparation of the invention may be incorporated is dairy products, such as yoghurt, chocolate and cereals.

Experiments

The experiments were conducted on 15 human volunteers experiencing symptoms of dyspepsia that did not disappear spontaneously. They were given 2 to 10 capsules per day containing algal meal produced by culturing of the algae *Haematococcus sp.* by AstaCarotene AB, Gustavsberg, Sweden. (These capsules are sold as an anti-oxidant and they contain 4 mg astaxanthin per capsule, with the instruction to take one capsule per day.)

This double to ten times the recommended dose, i.e. 8 - 40 mg astaxanthin per day, eliminated or drastically alleviated the symptoms of dyspepsia in all volunteers in 1 - 3 weeks, and no side effects were reported.

Astaxanthin from other sources, and other xanthophylls as well, are expected to be similarly useful for the purposes of the invention. An advantage of using astaxanthin from algae is, however, that the astaxanthin exists in a form esterified with fatty acids [Renström B. et al, 1981, Phytochem 20(11) :2561-2564], which esterified astaxanthin thereby is more stable during handling and storage than free astaxanthin.

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CLAIMS

1. Use of a at least one type of xanthophylls for the preparation of a medicament for prophylactic and/or therapeutic treatment of dyspepsia.

5 2. Use according to claim 1, wherein the xanthophyll is astaxanthin.

3. Use according to claim 2, wherein the astaxanthin is in a form esterified with fatty acids.

4. Use according to claim 3, wherein the astaxanthin in esterified form is provided in the form of algal meal prepared from a culture of the alga *Haematococcus sp.*

10 5. Use according to any one of claims 1 - 4, wherein the medicament further comprises carbohydrate structures.

6. Use according to any one of claims 1 - 5, wherein the medicament further comprises (a) different antioxidant(s).

15 7. Use according to any one of claims 1 - 6, wherein the medicament is in the form of unit doses adapted for a daily dosage of xanthophyll(s) in the range of 0.05 to 1 mg per kg body weight of an individual.

8. Method of prophylactic and/or therapeutic treatment of dyspepsia in an individual, which comprises administration to said individual of an dyspepsia-alleviating amount of a medicament comprising at least one type of xanthophylls.

20 9. Method according to claim 8, wherein the xanthophyll is astaxanthin.

10. Method according to claim 9, wherein the astaxanthin is in a form esterified with fatty acids.

11. Method according to claim 10, wherein the astaxanthin in esterified form is provided in the form of algal meal prepared from a culture of the alga *Haematococcus sp.*

25 12. Method according claim 8, wherein the medicament further comprises carbohydrate structures.

13. Method according to claim 8, wherein the medicament further comprises (a) different antioxidant(s).

30 14. Method according to claim 8, wherein the dyspepsia-alleviating amount of the medicament comprises xanthophyll(s) in the range of 0.05 to 1 mg per kg body weight of the individual.

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			U.S. Application Number (if known) 09/463958
International Application Number PCT/EP99/07551	International Filing Date October 8, 1999	Priority Date Claimed October 16, 1998	
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Applicant(s) for DO/EO/US Ake LIGNELL			

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14. ☐ A substitute specification.
15. ☐ A change of power of attorney and/or address letter.
16. ☐ Other items or information:

DECLARATION FOR PATENT APPLICATION AND APPOINTMENT OF ATTORNEY

As a below named inventor, I hereby declare that my residence, post office address and citizenship are as stated below next to my name; I believe that I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention (Design, if applicable) entitled:

TREATMENT OF DYSPEPSIA

the specification of (Attorney Docket REF/Lignell/551) which (check one):

☐ is attached hereto, or ☒ was filed on: **October 8, 1999** as PCT International Application Number: **PCT/EP99/07551**

and (if applicable) was amended on:

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment(s) referred to above. I acknowledge the duty to disclose information which is material to patentability as defined in *Title 37, Code of Federal Regulations, §1.56*. I hereby claim foreign priority benefits under *Title 35, United States Code §119* of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed.

PRIOR FOREIGN APPLICATION(S)			PRIORITY CLAIMED	
Number	Country	Day/Month/Year Filed	Yes	No
9803541-3	SE	16/10/98	X	

☐ Additional Priority Application(s) Listed on Following Page(s)

I HEREBY CLAIM THE BENEFIT UNDER TITLE 35 U.S. CODE §119(E) OF ANY U.S. PROVISIONAL APPLICATIONS LISTED BELOW.	
Application Number	Day/Month/Year Filed

☐ Additional Provisional Application(s) Listed on Following Page(s)

I hereby claim the benefit under *Title 35, United States Code, §120* of any United States application(s) or PCT international application(s) designating The United States of America listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in that/those prior application(s) in the manner provided by the first paragraph of *Title 35, United States Code, §112*, I acknowledge the duty to disclose information which is material to patentability as defined in *Title 37, Code of Federal Regulations, §1.56* which became available between the filing date of the prior application(s) and the national or PCT international filing date of this application:

Application Number	Filing Date	Status - Patented, Pending or Abandoned

☐ Additional US/PCT Priority Application(s) listed on Following Page(s)


I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under *section 1001 of title 18 of the United States Code* and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

POWER OF ATTORNEY: I (We) hereby appoint as my (our) attorneys, with full powers of substitution and revocation, to prosecute this application and transact all business in the Patent and Trademark Office connected therewith: J. Ernest Kenney, Reg. No. 19,179; Eugene Mar, Reg. No. 25,893; Richard E. Fichter, Reg. No. 26,382; Charles R. Wolfe, Jr., Reg. No. 28,680; Thomas J. Moore, Reg. No. 28,974; Joseph DeBenedictis, Reg. No. 28,502; Benjamin E. Urcia, Reg. No. 33,805; and

I(we) authorize my(our) attorneys to accept and follow instructions from STOCKHOLMS PATENTBYRA regarding any matter related to the preparation, examination, grant and maintenance of this application, any continuation, continuation-in-part or divisional based thereon, and any patent resulting therefrom, until I(we) or my(our) assigns withdraw this authorization in writing.

Send correspondence to: **BACON & THOMAS**
625 Slaters Lane - 4th Floor
Alexandria, VA 22314-1176

Telephone Calls to: (703) 683-0500

FULL NAME OF FIRST OR SOLE INVENTOR Ake LIGNELL	CITIZENSHIP Swedish
RESIDENCE ADDRESS Klippstigen 5 SE-139 00 Varmdo, SWEDEN SEX	POST OFFICE ADDRESS IS THE SAME AS RESIDENCE ADDRESS UNLESS OTHERWISE SHOWN BELOW
DATE 21/2/2000	SIGNATURE 

☐ See following page(s) for additional joint inventors.